

Efek pemberian ekstrak etanol biji delima (*punica granatum*) terhadap pertumbuhan dan ekspresi protein -catenin sel kanker kolorektal HCT116 = The effect of ethanol extract from pomegranate (*punica granatum*) seed on growth and expression of -catenin in colorectal cancer cell line HCT116

Nurul Mutmainna Yakub, author

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Abstrak

Pendahuluan: Kanker kolorektal adalah penyakit ganas tersering pada saluran pencernaan. Di Indonesia kanker kolorektal menempati urutan ketiga terbanyak dengan insidensi kasus sekitar 18 per 100.000 penduduk. Ekspresi berlebih -catenin dan penyimpangan jalur persinyalan -catenin berkorelasi dengan prognosis yang buruk pada penderita kanker kolorektal. Terapi kanker kolorektal yang dikembangkan saat ini adalah terapi target spesifik yaitu EGFR dan VEGF. Namun, pemberian terapi target spesifik menimbulkan berbagai efek samping seperti ruam, gatal, kulit kering, hidung berdarah, hipertensi, perforasi usus dan gangguan ginjal. Delima (*punica granatum*) adalah tanaman herbal yang diketahui memiliki sifat antioksidan dan anti-inflamasi. Efek delima sebagai antikanker telah diuji, namun penelitian mengenai biji delima terhadap kanker masih minim.

Metode: Ekstrak etanol biji delima (*Punica granatum*) dibuat dari serbuk kering biji buah delima melalui metode maserasi menggunakan pelarut etanol 96%. Efek ekstrak etanol biji delima (*Punica granatum*) terhadap ekspresi -catenin pada sel kanker kolorektal HCT116 dinilai melalui nilai H-score pada pewarnaan imunositokimia. Studi ini juga menilai potensi aktivitas dan efektivitas senyawa bioaktif *Punica granatum* untuk menghambat kanker kolorektal melalui jalur persinyalan -catenin menggunakan metode penambatan molekular.

Hasil: Penurunan ekspresi -catenin pada sel kanker kolorektal HCT116 dibuktikan dengan nilai rerata H-score sebesar 154,90 pada pemberian ekstrak etanol dengan dosis 200 ppm. Senyawa bioaktif coniferyl 9-O-[-D-apiofuranosyl(16)]-O--D-glucopyranoside, dan sinapyl 9-O-[-D-apiofuranosyl(16)]-O--D-glucopyranoside dapat menghambat kanker kolorektal melalui jalur persinyalan -catenin.

Kesimpulan: Biji delima (*Punica granatum*) terbukti menghambat pertumbuhan dan menurunkan ekspresi -catenin pada sel kanker kolorektal HCT116.

.....Introduction. Colorectal cancer is the most frequent malignancy in the gastrointestinal tract. In Indonesia, colorectal cancer placed third highest with an incidence of 18 per 100,000 population. Excessive expression of -catenin and deviation of -catenin signaling path correlate with poor prognosis of colorectal cancer patients. The currently developed colorectal cancer therapy is specific target therapy, i.e. EGFR and VEGF. However, it produces various side effects such as rash, pruritus, dry skin, nosebleed, hypertension, intestinal perforation and kidney disorder. Pomegranate (*Punica granatum*) is a herbal plant known to have anti-oxidant and anti-inflammatory properties. The effect of pomegranate as anti-cancer has been proven, however there are only a few studies regarding the effect of pomegranate seed on cancer.

Methods: Pomegranate (*Punica granatum*) seed ethanol extract was created from pomegranate seed dry powder made through maceration using 96% ethanol solvent. The effect of pomegranate (*Punica granatum*) seed ethanol extract on -catenin expression on HCT116 colorectal cancer cells was assessed using H-score

on immunohistochemistry staining. This study also assessed the activity and effectivity potential of Punica granatum bioactive substance in inhibiting colorectal cancer through β -catenin signaling path using molecular docking method.

Results: Decrease of β -catenin expression on HCT116 colorectal cancer cells was proven by the average H-score of 154.90 on administration of 200 ppm ethanol extract. Coniferyl 9-O-[β -D-apiofuranosyl(16)-O- β -D-glucopyranoside and sinapyl 9-O-[β -D-apiofuranosyl(16)]-O- β -D-glucopyranoside bioactive substances can inhibit colorectal cancer through β -catenin signaling path. Conclusion: Pomegranate (Punica granatum) seed was proven to inhibit the growth and decrease the expression of β -catenin on HCT116 colorectal cancer cells.